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Case Report

Double orifice mitral valve combined with left ventricular noncompaction in a child with Sotos syndrome

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ABSTRACT

Sotos syndrome is an autosomal dominant condition, sometimes complicated with cardiovascular malformations. We report the case of a 10-year-old Japanese male with Sotos syndrome found to have double orifice mitral valve (DOMV) combined with left ventricular noncompaction (LVNC) by transthoracic echocardiography. Three-dimensional echocardiography clearly demonstrated the trabecular meshwork, two separate mitral orifices with subvalvular apparatuses, and multiple tendinous cords. To the best of our knowledge, this is the first case of Sotos syndrome associated with DOMV and LVNC. Considering that mitral valve leaflets, chordae, papillary muscles, and primitive trabeculations of the left ventricle originate from the endomyocardial cushions in the developing heart, both cardiac defects in the present case might be explained by a common developmental aberrancy of endomyocardium. Patients with Sotos syndrome should be screened for mitral valve anomaly, subvalvular apparatuses, and left ventricular myocardial function as well as structural abnormalities.
<**Learning objective:** Sotos syndrome is sometimes complicated with cardiovascular malformations, including left ventricular noncompaction (LVNC) as reported in some previous articles. Considering the rarity of both the syndrome and LVNC, this combination might not be coincidental. It is intriguing that the present case had double orifice mitral valve in addition to LVNC, as both mitral valve leaflets and primitive trabeculations of LV might be derived in common from aberrant development of the endomyocardial cushions.>

Introduction

Sotos syndrome is characterized by typical facial appearance, childhood overgrowth with macrocephaly, and learning difficulties [1]. Several case reports have been published of this syndrome complicated with left ventricular noncompaction (LVNC) or double orifice mitral valve (DOMV) alone [2–4]. However, the combination of both complications has not been reported. In the present study, we show the case of Sotos syndrome associated with LVNC and DOMV.

Case report

A 10-year-old boy with Sotos syndrome was found to have heart murmur and referred to our hospital for echocardiographic evaluation. The patient was born at 37 weeks of gestation. Birth weight, height, and head circumference were 4270 g (+4.8SD), 56 cm (+4.9SD), and 38.5 cm (+4.3SD), respectively. The diagnosis of Sotos syndrome was based on the typical phenotypes, including almond-shaped eyes, hypertelorism, squint, wide forehead, pear-shaped head, childhood overgrowth with macrocephaly, and learning difficulties. However, gene analysis was negative for haploinsufficiency of the nuclear receptor Set Domain containing protein 1 gene (NSD1), which has been reported to be the cause of the syndrome [1]. The past medical history included coil embolization of ductus arteriosus at 3 years of age. Cardiac catheterization revealed that the ductus was small in diameter (2 mm) and pulmonary to systemic blood flow ratio was 1.1. The pulmonary arterial wedge pressure and left ventricular (LV) systolic/end-diastolic pressure were 7 and

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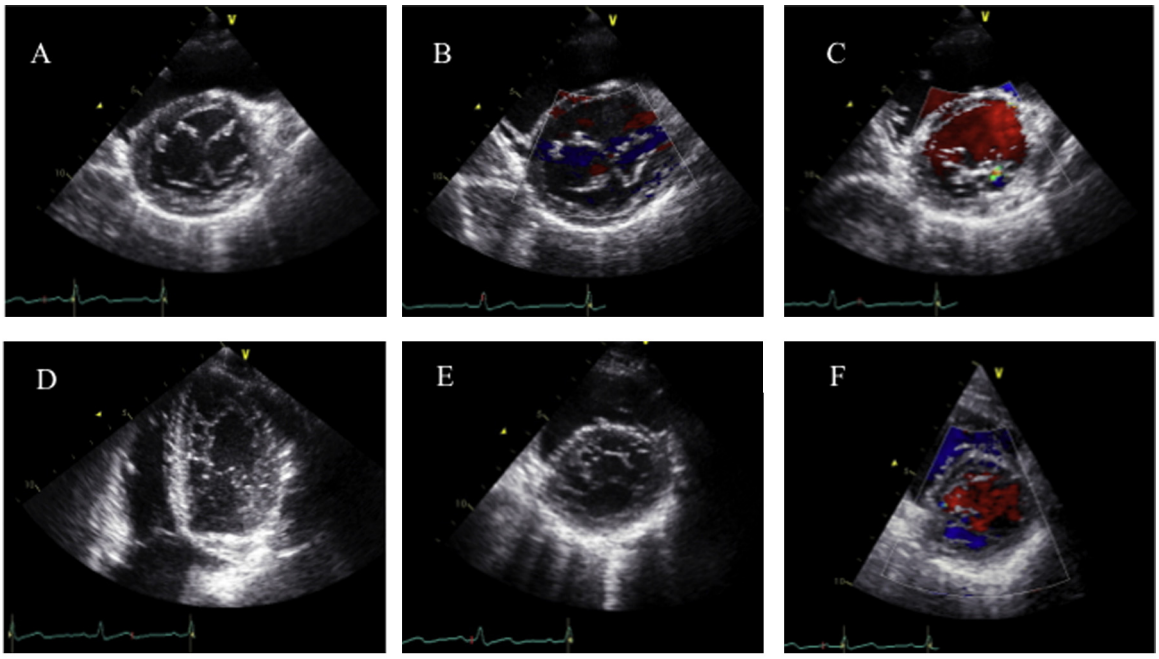

Fig. 1. Short-axis view of the mitral valve showed two mitral orifices (A), the presence of two separate inflow jets (B), and only minor mitral regurgitation (C). Left ventricular trabeculations encircled the endocardium at the apical and midportions with blood flows into the myocardial gaps on color Doppler imaging (D–F).

95/9 mmHg, respectively. Mitral valve inflow early filling velocity (E wave) and late filling velocity (A wave) were 127 and 88 cm/s on pulsed-Doppler echocardiography. Although slight mitral valve stenosis was suspected on these data, DOMV and LVNC went unnoticed at this stage.

At admission, chest auscultation showed normal heart sounds and only feeble diastolic murmur. No signs of heart failure were evident. A chest radiograph showed neither cardiomegaly (cardiothoracic ratio, 50%) nor lung congestion. Two-dimensional transthoracic echocardiography (TTE) showed two separate mitral valve orifices without stenosis (mean pressure gradient 1.5 mmHg for both), with trivial mitral regurgitation at the left orifice (Fig. 1A–C, Supplement 1). The areas of the two orifices were 1.9 (left) and 3.7 (right) cm^2. The LV end-diastolic volume and ejection fraction, calculated by the modified Simpson's method, were 87 ml/m^2 and 56%, respectively. LV trabeculations encircled the endocardium at the apical and midportions with blood flows into the myocardial gaps on color Doppler imaging (Fig. 1D–F, Supplement 2). Three-dimensional TTE showed the trabecular meshwork in short-axis view, with its own subvalvular apparatus and multiple tendinous cords (Fig. 2A and B, Supplement 3). Based on these findings, the final diagnosis was DOMV associated with LVNC.

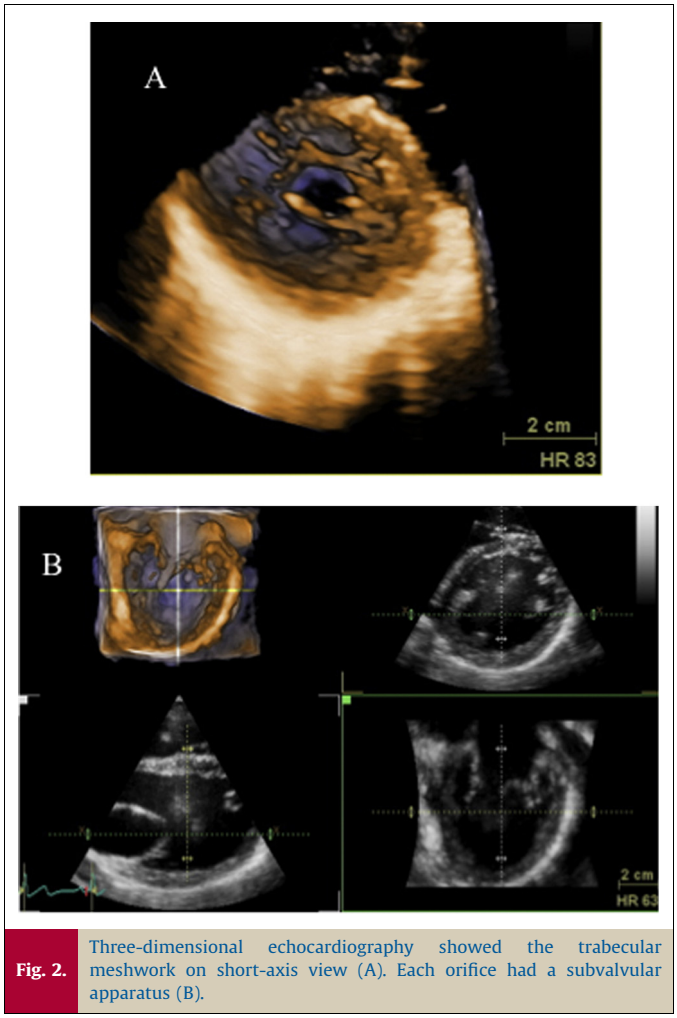

Fig. 2. Three-dimensional echocardiography showed the trabecular meshwork on short-axis view (A). Each orifice had a subvalvular apparatus (B).

Discussion

Sotos syndrome is an autosomal dominant condition characterized by typical facial appearance, childhood overgrowth with macrocephaly, and learning difficulties [1]. Haploinsufficiency of NSD1, due to intragenic mutations, and partial gene deletions or 5q35 microdeletions [2] have been reported as genetic causes of this syndrome. This syndrome is sometimes complicated with cardiovascular malformations. Although several case reports have been published of this syndrome complicated with LVNC or DOMV alone, the combination of both complications has not been reported previously [3,4]. LVNC is characterized by the persistence of embryonic myocardial morphology and thickening of LV wall in

the apical segments, due to noncompacted myocardium with prominent trabeculations [5]. LVNC is associated with heterogeneous genetic background, although the presence of any correlation with Sotos syndrome has not been firmly established [3,6]. In the present case, the patient showed no signs of cardiac failure. However, the patient had two mitral valve orifices due to the presence of central fibrous tissue and subvalvular apparatus, together with abnormal trabeculations at apical and midsegments.

In the developing heart, mitral valve leaflets, chordae and papillary muscles, as well as primitive trabeculations of the left ventricle, originate from the endomyocardial cushions. Thus, abnormal endomyocardial differentiation can result in both mitral anomalies and subvalvular structural diseases. Although the combination of DOMV and LVNC could be a coincidence considering the rarity of the diseases, it is intriguing that both abnormalities have been explained by developmental arrest of the endomyocardium. In fact, several cases with this combination have been reported in the literature [7–10].

Conclusions

To the best of our knowledge, this is the first case of Sotos syndrome associated with DOMV and LVNC. Patients with Sotos syndrome should be screened for mitral valve anomaly, subvalvular apparatuses, and LV myocardial abnormality and function due to the reported wide variability of cardiac symptoms [5,6].

Conflict of interest

None.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jccase.2014.11.002.

References

[1] Sotos JF, Dodge PR, Muirhead D, Crawford JD, Talbot NB. Cerebral gigantism in childhood. A syndrome of excessively rapid growth with acromegalic features and a nonprogressive neurologic disorder. N Engl J Med 1964;271:109–16.
[2] Kurotaki N, Imaizumi K, Harada N, Masuno M, Kondoh T, Nagai T, Ohashi H, Naritomi K, Tsukahara M, Makita Y, Sugimoto T, Sonoda T, Hasegawa T, Chinen Y, Tomita Ha HA, et al. Haploinsufficiency of NSD1 causes Sotos syndrome. Nat Genet 2002;30:365–6.
[3] Bano-Rodrigo A, Van Praagh S, Trowitzsch E, Van Praagh R. Double-orifice mitral valve: a study of 27 postmortem cases with developmental, diagnostic and surgical considerations. Am J Cardiol 1988;61:152–60.
[4] Martinez HR, Belmont JW, Craigen WJ, Taylor MD, Jefferies JL. Left ventricular noncompaction in Sotos syndrome. Am J Med Genet A 2011;155:1115–8.
[5] Niemann M, Liu D, Hu K, Cikes M, Beer M, Herrmann S, Gaudron PD, Hillenbrand H, Voelker W, Erti G, Weldemann F. Echocardiographic quantification of regional deformation helps to distinguish isolated left ventricular noncompaction from dilated cardiomyopathy. Eur J Heart Fail 2012;14:155–61.
[6] Moric-Janiszewska, Markiewicz-Łoskot G. Genetic heterogeneity of left-ventricular noncompaction cardiomyopathy. Clin Cardiol 2008;31:201–4.
[7] Demir F, Atalay S, Karadeniz C, Tutar E. Coexistence of left ventricular noncompaction and double-orifice mitral valve in a patient with congestive heart failure. Turk J Pediatr 2012;54:444–6.
[8] Wang XX, Song ZZ. A combination of left ventricular noncompaction and double orifice mitral valve. Cardiovasc Ultrasound 2009;7:11.
[9] Sugiyama H, Hoshiai M, Toda T, Nakazawa S. Double-orifice mitral valve associated with noncompaction of left ventricular myocardium. Pediatr Cardiol 2006;27:746–9.
[10] Gorgulu S, Celik S, Eksik A, Tezel T. Double-orifice mitral valve associated with nonisolated left ventricular noncompaction – a case report. Angiology 2004;55:707–10.